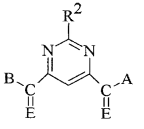
CLAIMS

What is claimed is:

1. A method for inhibiting matrix metalloproteinase enzymes in a mammal comprising administering an MMP inhibiting amount of a compound of Formula I



I

or a pharmaceutically acceptable salt thereof,

wherein:

R^2 is hydrogen, halo, hydroxy, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, NO_2, NR^4R^5, CN, or CF_3;

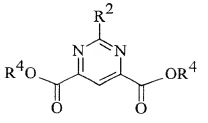
E is independently O or S,

A and B independently are OR^4 or NR^4R^5;

R^4 and R^5 independently are H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $(CH_2)_n$ aryl, $(CH_2)_n$ cycloalkyl, $(CH_2)_n$ heteroaryl, or R^4 and R^5 when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring, containing carbon atoms and optionally containing a heteroatom selected from O, S, or NH, and optionally substituted or unsubstituted;

n is an integer from 0 to 6.

2. A method for inhibiting matrix metalloproteinase enzymes in a mammal comprising administering an MMP inhibiting amount of a compound of Formula II



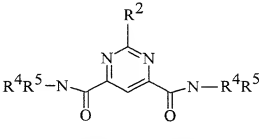
II

or a pharmaceutically acceptable salt thereof,

wherein R^2 is hydrogen, halo, hydroxy, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, NO_2, NR^4R^5, CN, or CF_3; and

each R^4 and R^5 independently are H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $(CH_2)_n$ aryl, $(CH_2)_n$ cycloalkyl, $(CH_2)_n$ heteroaryl, or R^4 and R^5 when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring, containing carbon atoms and optionally containing a heteroatom selected from O, S, or NH, and optionally substituted or unsubstituted.

3 A method for inhibiting matrix metalloproteinase enzymes in a mammal comprising administering an MMP inhibiting amount of a compound of Formula III



III

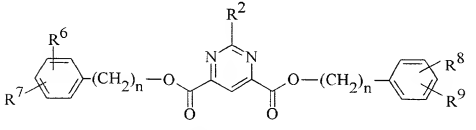
or a pharmaceutically acceptable salt thereof,

wherein R^2 is hydrogen, halo, hydroxy, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, NO_2, NR^4R^5, CN, or CF_3,

R^4 and R^5 independently are H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $(CH_2)_n$ aryl, $(CH_2)_n$ cycloalkyl, $(CH_2)_n$ heteroaryl, or R^4 and R^5 when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring containing carbon

atoms and optionally containing a heteroatom selected from O, S, or NH, and optionally substituted or unsubstituted.

4. A method for inhibiting matrix metalloproteinase enzymes in a mammal comprising administering an MMP inhibiting amount of a compound of Formula IV



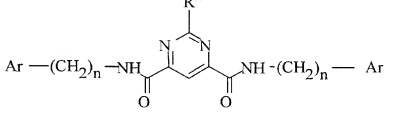
IV

or a pharmaceutically acceptable salt thereof,

wherein n is 0 to 6;

R^2 is hydrogen, halo, hydroxy, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, NO_2, NR^4R^5, CN, or CF_3; each R^4 and R^5 independently are H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $(CH_2)_n$ aryl, $(CH_2)_n$ cycloalkyl, $(CH_2)_n$ heteroaryl, or R^4 and R^5 when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring, containing carbon atoms and optionally containing a heteroatom selected from O, S, or NH. and optionally substituted or unsubstituted, and R^6, R^7, R^8, and R^9 independently are hydrogen, halo, C_1-C_6 alkyl, C_1-C_6 alkoxy, nitro, or NH_2

5. A method for inhibiting matrix metalloproteinase enzymes in a mammal comprising administering an MMP inhibiting amount of a compound of Formula V



V

or a pharmaceutically acceptable salt thereof,

wherein n is 0 to 6;

R^2 is hydrogen, halo, hydroxy, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, NO_2, NR^4R^5, CN, or CF_3;

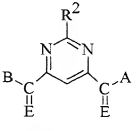
R^4 and R^5 independently are H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $(CH_2)_n$ aryl, $(CH_2)_n$ cycloalkyl, $(CH_2)_n$ heteroaryl, or R^4 and R^5 when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring, containing carbon atoms and optionally containing a heteroatom selected from O, S, or NH, and optionally substituted or unsubstituted;

Each Ar independently is aryl or Het,

Aryl is phenyl or substituted phenyl;

Het is an unsubstituted or substituted heteroaryl group

6. A compound having Formula I



I

or a pharmaceutically acceptable salt thereof,

wherein:

R^2 is hydrogen, halo, hydroxy, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, NO_2, NR^4R^5, CN, or CF_3,

E is independently O or S,

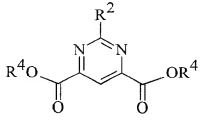
A and B independently are OR^4 or NR^4R^5;

R^4 and R^5 independently are H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $(CH_2)_n$ aryl, $(CH_2)_n$ cycloalkyl, $(CH_2)_n$ heteroaryl, or R^4 and R^5 when taken together with the nitrogen to which they are

attached complete a 3- to 8-membered ring containing carbon atoms and optionally containing a heteroatom selected from O, S, or NH, and optionally substituted or unsubstituted;

n is an integer from 0 to 6

7 A compound of Formula II



II

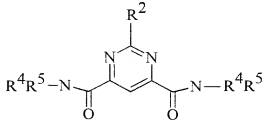
or a pharmaceutically acceptable salt thereof,

wherein R^2 is hydrogen, halo, hydroxy, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, NO_2, NR^4R^5, CN, or CF_3; and

each R^4 and R^5 independently are H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $(CH_2)_n$ aryl, $(CH_2)_n$ cycloalkyl, $(CH_2)_n$ heteroaryl, or R^4 and R^5 when taken together with a nitrogen to which they are both attached complete a 3- to 8-membered ring, containing carbon atoms and optionally containing a heteroatom selected from O, S, or NH, and optionally substituted or unsubstituted;

n is an integer from 0 to 6

8. A compound of Formula III



III

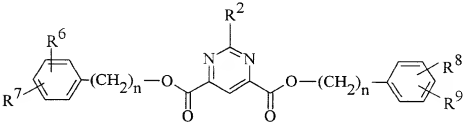
or a pharmaceutically acceptable salt thereof,

wherein R^2 is hydrogen, halo, hydroxy, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, NO_2, NR^4R^5, CN, or CF_3,

R^4 and R^5 independently are H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $(CH_2)_n$ aryl, $(CH_2)_n$ cycloalkyl, $(CH_2)_n$ heteroaryl, or R^4 and R^5 when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring containing carbon atoms and optionally containing a heteroatom selected from O, S, or NH, and optionally substituted or unsubstituted;

n is an integer from 0 to 6.

9 A compound of Formula IV



IV

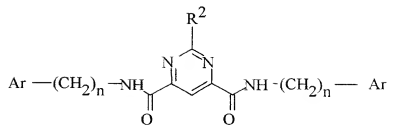
or a pharmaceutically acceptable salt thereof,

wherein Each n independently is an integer of from 0 to 6;

R^2 is hydrogen, halo, hydroxy, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, NO_2, NR^4R^5, CN, or CF_3; and R^6, R^7, R^8, and R^9 independently are hydrogen, halo, C_1-C_6 alkyl, C_1-C_6 alkoxy, nitro, or NH_2;

R^4 and R^5 independently are H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $(CH_2)_n$ aryl, $(CH_2)_n$ cycloalkyl, $(CH_2)_n$ heteroaryl, or R^4 and R^5 when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring containing carbon atoms and optionally containing a heteroatom selected from O, S, or NH, and optionally substituted or unsubstituted.

10. A compound of Formula V



V

or a pharmaceutically acceptable salt thereof,

wherein n is 0 to 6;

R^2 is hydrogen, halo, hydroxy, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, NO_2, NR^4R^5, CN, or CF_3;

R^4 and R^5 independently are H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $(CH_2)_n$ aryl, $(CH_2)_n$ cycloalkyl, $(CH_2)_n$ heteroaryl, or R^4 and R^5 when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring containing carbon atoms and optionally containing a heteroatom selected from O, S, or NH, and optionally substituted or unsubstituted

Each Ar independently is aryl or Het;

Aryl is phenyl or substituted phenyl;

Het is an unsubstituted or substituted heteroaryl group

11. A compound selected from:

Pyrimidine-4,6-dicarboxylic acid, (4-chloro-benzylamide), [(1,3-benzodioxol-5-ylmethyl)-amide];

Pyrimidine-4,6-dicarboxylic acid, (4-carboxy-benzylamide), [(1,3-benzodioxol-5-ylmethyl)-amide],

Pyrimidine-4,6-dicarboxylic acid, (4-carboxy-benzylamide), (4-methoxy-benzylamide),

Pyrimidine-4,6-dicarboxylic acid, (4-carboxy-benzylamide), (3-methoxy-benzylamide);

Pyrimidine-4,6-dicarboxylic acid, (4-carbomethoxy-benzylamide), (3-methoxy-benzylamide);

Pyrimidine-4,6-dicarboxylic acid, (4-carboxy-benzylamide), (3-pyridylmethylamide);

Pyrimidine-4,6-dicarboxylic acid, (4-carboxy-benzylamide), (3-thiophenemethylamide),

Pyrimidine-4,6-dicarboxylic acid, (2,1,3-benzothiadiazol-5-ylmethyl) amide, [(1,3-benzodioxol-5-ylmethyl)-amide],

Pyrimidine-4,6-dicarboxylic acid, (2,1,3-benzooxadiazol-5-ylmethyl) amide, [(1,3-benzodioxol-5-ylmethyl)-amide];

Pyrimidine-4,6-dicarboxylic acid, (2,1,3-benzothiadiazol-5-ylmethyl) amide, (4-methoxy-benzylamide);

Pyrimidine-4,6-dicarboxylic acid, (2,1,3-benzothiadiazol-5-ylmethyl) amide, (3-methoxy-benzylamide);

Pyrimidine-4,6-dicarboxylic acid bis-(1,3-benzodioxol-5-ylmethyl) ester,

Pyrimidine-4,6-dicarboxylic acid, bis-(4-chloro-benzylamide);

Pyrimidine-4,6-dicarboxylic acid, bis-[(1,3-benzodioxol-5-ylmethyl)-amide],

Pyrimidine-4,6-dicarboxylic acid, bis-(4-methoxy-benzylamide),

Pyrimidine-4,6-dicarboxylic acid, bis-(3-methoxy-benzylamide);

Pyrimidine-4,6-dicarboxylic acid, bis-(4-carboxy-benzylamide), and

Pyrimidine-4,6-dicarboxylic acid, bis-(4-carbomethoxy-benzylamide)

12. A pharmaceutical composition, comprising an MMP-13 inhibiting amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier, diluent, or excipient.

13. The pharmaceutical composition according to Claim 12, comprising an MMP-13 inhibiting amount of a compound of Formula II, or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier, diluent, or excipient

14 The pharmaceutical composition according to Claim 12, comprising an MMP-13 inhibiting amount of a compound of Formula III, or a

pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier, diluent, or excipient.

15. The pharmaceutical composition according to Claim 12, comprising an MMP-13 inhibiting amount of a compound of Formula IV, or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier, diluent, or excipient

16. The pharmaceutical composition according to Claim 12, comprising an MMP-13 inhibiting amount of a compound of Formula V, or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier, diluent, or excipient.

17. The pharmaceutical composition according to Claim 12, comprising a compound selected from:

Pyrimidine-4,6-dicarboxylic acid, (4-chloro-benzylamide), [(1,3-benzodioxol-5-ylmethyl)-amide];

Pyrimidine-4,6-dicarboxylic acid, (4-carboxy-benzylamide), [(1,3-benzodioxol-5-ylmethyl)-amide],

Pyrimidine-4,6-dicarboxylic acid, (4-carboxy-benzylamide), (4-methoxy-benzylamide),

Pyrimidine-4,6-dicarboxylic acid, (4-carboxy-benzylamide), (3-methoxy-benzylamide),

Pyrimidine-4,6-dicarboxylic acid, (4-carbomethoxy-benzylamide), (3-methoxy-benzylamide),

Pyrimidine-4,6-dicarboxylic acid, (4-carboxy-benzylamide), (3-pyridylmethylamide);

Pyrimidine-4,6-dicarboxylic acid, (4-carboxy-benzylamide), (3-thiophenemethylamide);

Pyrimidine-4,6-dicarboxylic acid, (2,1,3-benzothiadiazol-5-ylmethyl) amide, [(1,3-benzodioxol-5-ylmethyl)-amide];

Pyrimidine-4,6-dicarboxylic acid, (2,1,3-benzooxadiazol-5-ylmethyl) amide, [(1,3-benzodioxol-5-ylmethyl)-amide],

Pyrimidine-4,6-dicarboxylic acid, (2,1,3-benzothiadiazol-5-ylmethyl) amide, (4-methoxy-benzylamide);

Pyrimidine-4,6-dicarboxylic acid, (2,1,3-benzothiadiazol-5-ylmethyl) amide, (3-methoxy-benzylamide);

Pyrimidine-4,6-dicarboxylic acid bis-(1,3-benzodioxol-5-ylmethyl) ester;

Pyrimidine-4,6-dicarboxylic acid, bis-(4-chloro-benzylamide),

Pyrimidine-4,6-dicarboxylic acid, bis-[(1,3-benzodioxol-5-ylmethyl)-amide];

Pyrimidine-4,6-dicarboxylic acid, bis-(4-methoxy-benzylamide);

Pyrimidine-4,6-dicarboxylic acid, bis-(3-methoxy-benzylamide);

Pyrimidine-4,6-dicarboxylic acid, bis-(4-carboxy-benzylamide), and

Pyrimidine-4,6-dicarboxylic acid, bis-(4-carbomethoxy-benzylamide), or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier, diluent, or excipient

18. A method for inhibiting an MMP-13 enzyme in an animal, comprising administering to the animal an MMP-13 inhibiting amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof.

19. A method for treating a cancer, comprising administering to a patient having cancer and in need of treatment an anticancer effective amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof.

20 A method for treating breast carcinoma, comprising administering to a patient having cancer and in need of treatment an anticancer effective amount of a compound of Formula I. or a pharmaceutically acceptable salt thereof

21. A method for treating heart failure, comprising administering to a patient in need of treatment an effective amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof.

22. A method for treating inflammation, comprising administering to a patient in need of treatment an effective amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof.

23. A method for treating osteoarthritis, comprising administering to a patient in need of treatment an effective amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof.

24. A method for treating rheumatoid arthritis, comprising administering to a patient in need of treatment an effective amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof.

25. A method of treating a disease or disorder selected from cancer, heart failure, inflammation, rheumatoid arthritis, and osteoarthritis, comprising administering to a patient in need of treatment an effective amount of a compound of Formula II, III, IV, or V, or a pharmaceutically acceptable salt thereof.